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**European Commission Approves SYLVANT<sup>®</sup> (siltuximab) as a Treatment for Patients with Multicentric Castleman’s Disease (MCD)**

***First treatment approved for the management of MCD in Europe***

Beerse / Belgium, June 4, 2014 – Janssen-Cilag International NV (“Janssen”) announced today that the European Commission (EC) has approved the use of SYLVANT<sup>®</sup> (siltuximab) for the treatment of adult patients with multicentric Castleman’s disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpes virus-8 (HHV-8) negative.<sup>1</sup> SYLVANT is a monoclonal antibody (a specialised type of protein) that binds selectively to an antigen in the body called interleukin-6 (IL-6). SYLVANT is administered as an intravenous (IV) infusion once every three weeks<sup>2</sup> and is the first medicine to receive regulatory approval in the EU for the treatment of MCD patients.

MCD is a rare blood disorder with high morbidity in which lymphocytes, a type of white blood cells, are over-produced, leading to enlarged lymph nodes. MCD can also affect lymphoid tissue of internal organs, causing the liver, spleen, or other organs to enlarge.<sup>3</sup> Infections, multisystem organ failure and malignancies including malignant lymphoma are common causes of death in patients with MCD.<sup>3,4</sup> It is classified as a rare disease by the European Commission, meaning that it affects fewer than five in 10,000 people.<sup>5</sup> In fact, MCD is so rare that it is difficult to track the number of cases across Europe. As the majority of publications on MCD are based on case reports, epidemiological evidence is very scarce. However, a recent study from the U.S. estimated the 10-year prevalence of MCD to be 2.4 cases per million inhabitants.<sup>6</sup>

“The approval of SYLVANT means that there is now an EU approved treatment for patients with MCD who are HIV negative and HHV-8 negative. SYLVANT will provide an urgently needed treatment



option that will make a significant difference to the way that MCD is managed," said Professor Pier Luigi Zinzani, Associate Professor of Hematology, University of Bologna, Italy. "It has the potential to become a new standard of care for patients, providing an important new therapeutic option to those suffering with this chronic, serious and debilitating disease."

While the cause of MCD currently is unknown, overproduction of IL-6 is considered a key mechanism in MCD.<sup>3,7</sup> SYLVANT works by binding to human IL-6, a multifunctional cytokine produced by various cells such as T cells, B cells, monocytes, fibroblasts and endothelial cells.<sup>2,7</sup>

Jane Griffiths, Company Group Chairman of Janssen Europe, the Middle East and Africa (EMEA) said, "Janssen is committed to developing compounds in areas of unmet medical need and our expertise in haematologic malignancies was key to recognising the potential of SYLVANT. As the first company with an approved medicine to treat MCD in Europe, we are very proud to be able to offer an effective treatment option for eligible patients with this rare and challenging disease and further demonstrate our commitment to patients."

The EC approval was based on the results of the MCD2001 Pivotal Study and follows the accelerated assessment and recommendation from the CHMP to approve SYLVANT<sup>®</sup> on March 20, 2014. The U.S. Food and Drug Administration's approval of SYLVANT<sup>™</sup> was announced on April 23, 2014. SYLVANT has been granted orphan drug status for MCD in both the EU and the United States (U.S.).

### **About the study**

The efficacy and safety of SYLVANT were evaluated in a multi-national, randomised, double-blind, placebo-controlled pivotal study in 79 patients with MCD (MCD2001). MCD2001 is the first randomised study in MCD.<sup>8</sup> Fifty-three patients were randomised to the SYLVANT arm at a dose of 11 mg/kg every 3 weeks and 26 patients were randomised to the placebo arm. Patients had symptomatic MCD and were HIV negative and HHV-8 negative.<sup>2,8</sup>

Treatment of MCD tumours and related symptoms is an important treatment goal for these patients. In this pivotal study, which led to the European Commission approval, more than one-third of patients in the SYLVANT arm had a durable tumour and symptomatic response to treatment plus best supportive care (BSC), compared to none of the patients who received placebo plus BSC (34 percent versus 0 percent according to stringent criteria; 95 percent CI: 11.1, 54.8; p=0.0012). A durable response was defined as tumour and symptomatic response (reduction in tumour size and complete resolution or stabilisation of disease symptoms) that persisted for a minimum of 18 weeks without treatment failure. The median time to treatment failure was not reached for patients who



received SYLVANT plus BSC; those who received placebo plus BSC experienced treatment failure at a median of 134 days ( $p=0.0084$ ). Efficacy results from MCD2001 also showed tumor response for those in the SYLVANT arm was 37.7 percent versus 3.8 percent for those in the placebo arm ( $p=0.0022$ ). Among anaemic patients, an increase in hemoglobin of at least 15 g/L at week 13 was seen in 61.3 percent of patients in the SYLVANT arm versus 0 percent in patients who received placebo and BSC ( $p=0.0002$ ).<sup>2,8</sup> (Note. SYLVANT was not studied in patients with MCD who are HIV positive or HHV-8 positive because it did not bind to virally produced interleukin-6 (IL-6) in a nonclinical study.)

### **About SYLVANT® (siltuximab)**

SYLVANT is an anti-interleukin-6 (IL-6) chimeric monoclonal antibody that binds to human IL-6.<sup>2</sup> IL-6 is a multifunctional cytokine produced by various cells such as T cells, B cells, monocytes, fibroblasts and endothelial cells. Dysregulated overproduction of IL-6 from activated B cells in affected lymph nodes has been implicated in the pathogenesis of, or mechanism causing, MCD.<sup>7</sup> Information about ongoing studies with siltuximab can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **About multicentric Castleman's disease (MCD)**

MCD is a rare blood disorder with high morbidity in which lymphocytes, a type of white blood cell, are over-produced and lead to enlargement of lymph nodes. MCD can also affect lymphoid tissue of internal organs, causing the liver, spleen or other organs to enlarge.<sup>3</sup> MCD signs and symptoms are driven by dysregulated IL-6 production.<sup>3,7</sup> Some symptoms can be life threatening.<sup>3,4</sup>

Unlike "unicentric" Castleman's disease, which is localised and affects only a single area or group of lymph nodes, patients with MCD have more than one group of lymph nodes in different anatomical areas that are affected. Unicentric disease can be treated by surgically removing the diseased lymph node, while multicentric disease is usually much more difficult to treat.<sup>3,7</sup>

### **About Janssen**

Janssen Pharmaceutical Companies of Johnson and Johnson are dedicated to addressing and solving the most important unmet medical needs of our time, including oncology (e.g. multiple myeloma and prostate cancer), immunology (e.g. psoriasis), neuroscience (e.g. schizophrenia, dementia and pain), infectious disease (e.g. HIV/AIDS, hepatitis C and tuberculosis), and cardiovascular and metabolic diseases (e.g. diabetes). Driven by our commitment to patients, we develop sustainable,



integrated healthcare solutions by working side-by-side with healthcare stakeholders, based on partnerships of trust and transparency. More information can be found on [www.janssen-emea.com](http://www.janssen-emea.com). Follow us on [www.twitter.com/janssenEMEA](http://www.twitter.com/janssenEMEA) for our latest news.

### **Janssen in Oncology**

In oncology, our goal is to fundamentally alter the way cancer is understood, diagnosed, and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include a focus on haematologic malignancies, prostate cancer and lung cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualised use of our therapies; as well as safe and effective identification and treatment of early changes in the tumor microenvironment.

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*(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995, including those regarding expectations for SYLVANT<sup>®</sup> (siltuximab). The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in new product development, including obtaining regulatory approvals; challenges to patents; competition, including technological advances, new products and patents attained by competitors; changes in behavior and spending patterns or financial distress of purchasers of health care products and services; changes to governmental laws and regulations and domestic and foreign health care reforms; and general industry conditions including trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2013, including in Exhibit 99 thereto, and our subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at [www.sec.gov](http://www.sec.gov), [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. None of the Janssen Pharmaceutical*



Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.)

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